Symptomatic Second-Degree Atrioventricular Block Due to Thalidomide

Talidomide Bağlı Semptomatik 2. Derece Atriyoventriküler Blok

Atrioventricular Block and Thalidomide

Hakki Kaya, Recep Kurt
Departments of Cardiology, Cumhuriyet University Medical School, Sivas, Turkey

Bu olgu 3. Kardiyobahar güncellemesinde bildiri olarak kabul edilmiş ve sunulmuştur.

Özet

Talidomid antiinflamatuar, antiangiogenetik ve immünomodulator etkilerinden dolayı günümüzde çeşitli hastalıklarda artan oranda kullanılmaktadır . Talidomidin sinüzal bradikardi yapabildiği ile ilgili çalışmalar mevcuttur. Sadece bir vakada ise talidomidle ilişkili atrioventriküler(AV) tam blok bildirilmiştir. Ancak şu ana kadar talidomid ile ilgili 2. Derece AV blok olgusu bildirilmemiştir. Burada, 50 yaşında, multipl myleom nedeniyle talidomid kullanmakta olan, acil servise senkop ile başvuran ve 2:1 AV blok saptanan bir hastayı sunmaktayız. Hastanın son 5 aydır 100 mg /gün talidomid kullandığı ve ilaç başlanmadan önceki elektrokardiyografilerinde anormal bir bulgu olmadığı görüldü. Başvuru anında hastanın kalp hızı 45-75/dk arasında değişmekteydi. Hastanın hipotansiyona eşlik eden senkobu olması nedeniyle geçici kalp pili implante edildi. Talidomid tedavisi sonlandırıldıktan 5 gün sonra hastanın kalp hızının 80/dk olduğu izlendi ve ertesi gün geçici pacemaker çıkarıldı. Geçici pacemaker çıkarıldıktan sonra yapılan ritm holterde anormal bulgu izlenmedi. Talidomid kullanan hastalarda yakın kardiyak ve elektrokardiyografik takip yapılmalıdır.

Anahtar Kelimeler

Atriyoventriküler Blok; Senkop; Talidomid; Multiple Myelom

Abstract

Due to its anti-inflammatory, anti-angiogenic, and immunomodulatory effects, thalidomide is increasingly used in the treatment of various diseases. Previous studies have demonstrated that thalidomide may cause sinusal bradycardia. Thalidomide-associated complete atrioventricular block has been reported in only a single case, but there is no case of second-degree atrioventricular block associated with thalidomide in the literature. Here, we present the case of a 50-year-old patient who had been using thalidomide for multiple myeloma. The patient was admitted to the emergency service with syncope, and had second-degree (2:1) atrioventricular block. The patient was using thalidomide (100 mg/day) for the previous 5 months and had not had any abnormal findings in previous electrocardiographies. His heart rate on presentation was variable, from 45 to 75 bpm. He was treated with a temporary pacemaker because of hypotension and syncope. Five days after the completion of the thalidomide treatment, the patient's heart rate was 80 bpm. The following day, the pacemaker was removed and a Holter ECG did not show any abnormalities. Patients undergoing thalidomide treatment should be followed up for cardiac and electrocardiographic parameters.

Keywords

Atrioventricular Block; Syncope; Thalidomide; Multiple Myeloma

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Corresponding Author: Hakki Kaya, Departments of Cardiology, Cumhuriyet University Medical School, Sivas, Turkey.
T.: +90 3462581807 F.: +90 3462191268 E-Mail: drhakkikaya84@gmail.com

Introduction

Thalidomide, originally developed as an antiemetic drug for pregnant women, was taken off the market because of its teratogenic effects. Because of the anti-angiogenetic effects and suppression of TNF-alpha, thalidomide has reemerged for investigational purposes in the treatment of various inflammatory conditions (erythema nodosum leprosum, cutaneous lupus erythematosus, rheumatoid arthritis, Behcet's and Crohn's disease, graft versus host disease, refractory aphthous ulcerations in HIV patients) and various cancers (multiple myeloma, lymphomas, Karposi's sarcoma, renal cell, urothelial, and hepatocellular carcinomas) [1].

Case Report

A 50-year-old male patient with no prior cardiovascular history was admitted to the hospital complaining of syncope and weakness. There was no chest pain or palpitation. His pulse was found to average 60 beats per minute (bpm) and his blood pressure was 80/50 mmHg. Cardiac examination revealed no S3 or S4 gallops and no other heart murmurs. The chest X-ray was normal. The laboratory tests showed normal kidney, liver, and thyroid function, and cardiac enzyme and electrolytes, with normocytic anemia of Hb 9.0 g/dL. The electrocardiogram revealed Type II second-degree atrioventricular block with a variable ventricular rate from 45 to 75 bpm (Figure 1). A temporary

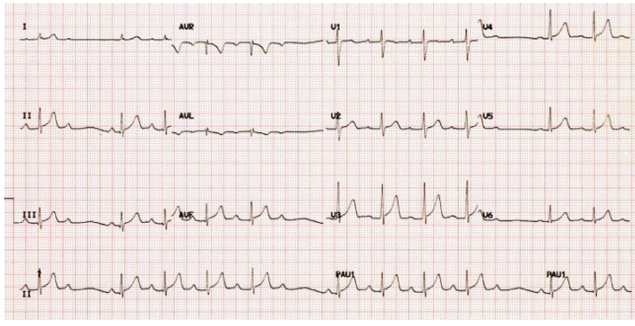

Figure 1. ECG at the time of admission to the hospital

pacemaker was implanted via the internal jugular vein to provide ventricular stimulation at 80 bpm. The blood pressure returned to normal with recovery of the patient. The echocardiogram showed both atrial enlargements with normal ventricular systolic function and an ejection fraction of 60%.

The patient had been followed for his multiple myeloma diagnosis for 3 years and had been using thalidomide (100 mg/day) for the previous 5 months. The patient underwent a myocardial biopsy, which showed no sign of amyloidosis. The patient was not using any other medication or treatment. Previous electrocardiograms had revealed no conduction abnormalities. Coronary angiography showed normal coronary arteries with no obstructive lesions.

Due to previous reports of thalidomide-associated bradycardia, thalidomide treatment was discontinued. The patient's heart rate was 80 bpm on day 5, and in normal sinus rhythm. The temporary pacemaker was removed on the sixth day of hospitalization. After removal of the pacemaker, Holter ECG showed no abnormality. He was discharged on the eighth day of hospitalization.

Discussion

Thalidomide has a number of well-recognized side effects such as teratogenicity, skin rash, peripheral neuropathy, pneumonitis, and venous thromboembolism. Post-marketing data reported a 0.12% rate of thalidomide-induced bradycardia, but recent reports demonstrate that thalidomide-induced bradycardia may be more frequent, up to 5%-53% [2]. Except for one case with complete atrioventricular block, all reported cases are sinusal bradycardia [3,4]. There is no case of second-degree atrioventricular block associated with thalidomide in the literature.

The mechanism by which thalidomide causes bradycardia has not yet been determined. Thalidomide treatment can cause hypothyroidism [5]. In our case, the patient had normal thyroid hormone levels; therefore, this is not sufficient to explain 2:1 atrioventricular block. The most plausible mechanism is related to thalidomide-associated decrease in TNF-α levels [6]. Emch and his colleagues reported that TNF- α inhibits activity of the dorsal motor nucleus of the vagus nerve that supplies visceral parasympathetic fibres to the heart [7]. By this means, thalidomide could lead to overactivity of the parasympathetic system, resulting in bradycardia or block because of the reduced TNF-α levels [3].

Due to its anti-angiogenic, immunomodulating, and anti-inflammatory effects, thalidomide is increasingly used in the treatment of hematological diseases, autoimmune diseases, and cancer. As thalidomide is prescribed more frequently, clinicians should be aware of the possibility of thalidomide-induced bradycardia. Cardiac monitoring should be instituted and electrocardiographic parameters should be screened when treating patients with thalidomide. Regular ECGs should be performed when rate disturbance is noted while patients are on this drug.

Competing interests

The authors declare that they have no competing interests.

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